June 27, 2002

Courtney M. Price, Vice President
CHEMSTAR
American Chemistry Council Fatty Nitrogen Derivatives Working Group
1300 Wilson Boulevard
Arlington, VA 22209

Dear Ms. Price:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the Fatty Nitrogen Derivatives Amides category, posted on the ChemRTK HPV Challenge Program Web site on January 11, 2002. I commend American Chemistry Council Fatty Nitrogen Derivatives Working Group for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its HPV Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the attached Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that American Chemistry Council Fatty Nitrogen Derivatives Working Group advise the Agency, within 90 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@.epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Fatty Nitrogen Derived Amides Category

SUMMARY OF EPA COMMENTS

The sponsor, the American Chemistry Council Fatty Nitrogen Derivatives Amides Task Group, submitted a test plan and robust summaries to EPA for the Fatty Nitrogen Derived (FND) Amides chemical category dated November 27, 2001. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 11, 2002. The category consists of 28 members plus 6 non-HPV chemicals as supporting substances.

EPA believes that the category as proposed by the submitter is not adequately supported. There were many inadequacies in the test plan and in robust summaries, which need to be addressed to be minimally acceptable for the HPV Challenge Program. The submitter needs to provide a strong basis for grouping the chemicals in each of the subcategories and also for extrapolating data among category members.

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

EPA COMMENTS ON THE FATTY NITROGEN DERIVED AMIDES CATEGORY CHALLENGE SUBMISSION

Category Justification. The fatty nitrogen derived amides category includes a range of structures such as amides, amine salts, imidazoles, and quaternary ammonium salts. The submitter divides the category into four subcategories containing both single compounds and mixtures. Some of the mixtures are potentially complex, variable composition reaction products or mixtures derived from tall oil or other natural products. For example, Subcategory II is made up of products of the reaction of various fatty acid mixtures with a variety of amines. The submitter does not characterize these "reaction products," which could be amides or salts or mixtures of both, or even other types of substances depending on the reaction conditions, beyond the statement that "Subcategory II chemicals, in many cases, contain Subcategory I chemicals as major components." For all subcategories, the submitter needs to address the identity and composition of each member in sufficient detail for reviewers to evaluate its approach for grouping these divergent chemical structures into one category.

The submitter plans to extrapolate the available test data from one subcategory to another. It is not clear why subcategories were created if the submitter did not plan to characterize each one separately. The subcategory issue is further complicated by the fact that the largest subcategory, Subcategory I, is highly diverse structurally compared to the others, and the submitter does not address the problems thus created. It is also unclear, for example, why a subcategory dominated by N-(mono or bis)-2-hydroxyethylamides should also contain simple primary amides and even an N-(N,N-dimethylaminopropyl)amide.

Test Plan. Some studies are provided for selected category members, mainly for chemicals in subcatagories I and IV of the test plan. However, data are not available for many other chemicals, especially in subcategories II and III. For members that lack test data, the submitter proposes that adequate information is available through "read-across" from the existing or proposed testing. The submitter, however, does not provide adequate justification in the submission to support extrapolation of the submitted data to the other members of the category. The submitter also does not provide a rationale that supports a pattern of physicochemical properties, environmental fate properties, aquatic toxicity or health effects across the category or subcategories. It is likely that additional testing will be needed for the purposes of the HPV Challenge Program.

The submitter needs to consider dispersibility vs. water solubility of these substances when designing ecological testing.

Robust Summaries

While EPA has not completed its technical review of this submission, it has the following preliminary comments:

Most of the health effects robust summaries provided enough detail on experimental methods and results to allow independent evaluation of the reliability of the studies. However, some robust summaries omit important experimental details that should be included, such as test substance purity, administered doses, mortality, clinical signs, and necropsy results.

Few of the ecotoxicity robust summaries provided sufficient experimental and methodological details and results to allow independent evaluation of study adequacy. Many robust summaries are missing important details such as test substance purity, test concentrations, numbers of test organisms per concentration, water quality data, culture medium data, statistical methods, and concentration- and duration-response data.

The sponsor needs to provide robust summaries for the ECOSAR predictions including all input values and model parameters.

Followup Activity

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.